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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,756	12/30/2004	Johan Neyts	50304/054001	5115
21559	7590	09/09/2009	EXAMINER	
CLARK & ELBING LLP			WANG, SHENGJUN	
101 FEDERAL STREET			ART UNIT	
BOSTON, MA 02110			PAPER NUMBER	
			1617	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No. 10/519,756	Applicant(s) NEYTS ET AL.	
	Examiner Shengjun Wang	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 May 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23-29, 50 and 51 is/are pending in the application.
- 4a) Of the above claim(s) 26 and 27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23-25, 28, 29, 50 and 51 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>5/15/2009</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Receipt of applicants' amendments and remarks submitted May 15, 2009 is acknowledged.

Claim Rejections 35 U.S.C. 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 23-29 and 51-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment with the compounds defined therein, isomer or salts thereof, does not reasonably provide enablement for solvates of these compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

3. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ 2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factor to consider when assessing if a disclosure would have required undue experimentation. The court recited eight factors:

- 1) the quantity of experimentation necessary,
- 2) the amount of direction or guidance provided,
- 3) the presence of absence of working examples,
- 4) the nature of the invention,

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- 5) the state of the prior art,
- 6) the relative skill of those in the art,
- 7) the predictability of the art, and
- 8) the breadth of the claims.

Factual Basis:

The Specification has no working example of solvate for a compound of formula (Z); and some of the exemplified compounds within the claimed genus were in contact with solvent. Yet no evidence has shown a solvate that deemed to be useful in the claimed method.

Searching general area of solvates resulted in a pertinent reference by West *et al* (Solid Solutions, Solid State Chemistry and its applications, 1986). West shows a lack of predictability of the art in the solvate area.

Based on these two facts, a scope of enablement rejection follows using relevant Wands factors. Hence, the burden of establishing a *prima facie* case is met.

The Nature of the invention and the state of the prior art:

The invention is drawn to the employment of compounds according to formula (Z), or a pharmaceutically acceptable salt, isomer or solvate thereof. The specification is not adequately enabled as to how to make solvates, for the compounds according to formula (Z); the specification has no examples of solvates of the instantly employed compounds. The compounds of formula (Z) embrace bicyclical heterocyclic compounds substituted with a variety of substitutes. Careful calculation of the number of compounds embraced in the instantly claimed formula (I) shows a large number of compounds. The term "substituted" (in all occurrences)

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embraces undefined number of variable groups and thus, the genus embraced by Claim 1 is excessively large and there is no teaching of any hydrate, or solvate of this large genus.

4. Search in the pertinent art, including water a solvent resulted in a pertinent reference, which is indicative of unpredictability of solvate formation in general. The state of the art is that it is not predictable whether solvates will form or what their composition will be. In the language of the physical chemist, a solvate of an organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph on page 358 of the West reference. The solvent molecule is a species introduced into the crystal and no part of the organic host molecule is left out or replaced. In the first paragraph on page 365, West states, "it is not usually possible to predict whether solid solutions will form, or if they do form what is the compositional extent." Thus, in the absence of experimentation one cannot predict if a particular solvent will solvate any particular crystal. One cannot predict the stoichiometry of the formed solvate, i.e. if one, two, or a half a molecule of solvent added per molecule of host. Compared with polymorphs, there is an additional degree of freedom to solvates, which means a different solvent or even the moisture of the air that might change the stable region of the solvate. In the instant case of solvate a similar reasoning therefore applies. Water is a solvate and hence it is held that a pertinent detail of West, which relates to solvates, is also applicable to water.

5. Furthermore, an additional search resulted in Vippagunta et al. (Advanced Drug Delivery Reviews, 48, 3-26, 2001), which clearly states that formation of solvates is unpredictable. See entire document, especially page 18, left column: section 3.4. Vippagunta et al states, "Each solid compound responds uniquely to the possible formation of solvates or hydrates and, hence,

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generalizations cannot be made for series of related compounds." Ulrich (Chapter 4 in Crystallization, Kirk-Othmer Encyclopedia of Chemical Technology) provides that "Pseudopolymorphs are solvates or in the case of water as solvent, hydrates, which means crystals that incorporate solvent molecules into the crystal lattice. Pseudopolymorphs exhibit different crystal forms and/or different densities, solubilities, dissolution rates, colors, hardness, etc. Compared with polymorphs, there is an additional degree of freedom (than temperature and pressure), which means a different solvent or even the moisture of the air that might change the stabile region of the pseudopolymorph."

The predictability or lack thereof in the art:

6. The solvate as applied to the above-mentioned compounds employed by the applicant are not art-recognized compounds and hence, there should be adequate enabling disclosure in the specification with working examples. The amount of direction or guidance present:

Examples illustrated in the experimental section are limited to making the compounds and not related to solvates thereof. There is no example of the instantly employed compound being characterized as a solvate. Many of the exemplified compounds were shown in the specification that have come in contact with water and/or other solvents; however, there is no showing that these compounds formed hydrates, or solvates. Therefore, it is clear that merely bringing the compound and water or solvent together does not result in solvate and additional direction or guidance is needed to make them.

The presence or absence of working examples:

7. Determining if any particular substrate would form a solvate, or hydrate would require synthesis of the substrate and subjecting it to recrystallization with a variety of solvents,

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temperatures, and other parameters. The experimentation is potentially open-ended. The application fails provide working example, guidance or direction as to how to making the solvate and hydrate encompassed herein. These cannot be Simply willed into existence. As was stated in Morton International Inc. v. Cardinal Chemical Co., 28 USPQ2d 1190 "[T]he specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However... there, is no evidence that such compounds exist..., the examples of the patent do not produce the postulated compounds..., there is... no evidence that such compounds even exist." The same circumstance appears to be true here. There is no evidence that solvates of these compounds actually exist; if they did, they would have formed. There should be some showing supporting that solvates of these compounds exist and therefore can be made.

The breadth of the claims and the quantity of experimentation needed:

The specification provides no support, as noted above, for compounds generically embraced in Claim 1, which would lead to a desired solvate of the compounds according to formula (Z). As noted above, the genus embraces a large number of compounds, and therefore the claims are broad. The quantity of experimentation needed would be an undue burden on one skilled in the chemical art since there is inadequate guidance given to the skilled artisan for the many reasons stated above. Even with the undue burden of experimentation, there is no guarantee that one would get the product of desired solvate of compounds of formula (I) embraced in the instant claims in view of the pertinent reference teachings.

For the reasons discussed above, the claims are not enabled in the aspect of the solvate.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 23-29 and 52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 23, for defining R3, recites the broad recitation "heterocyclic," and the claim also recites "oxyheterocyclic" and "thioheterocyclic" which is the narrower statement of the range/limitation.

Remarks

11. Applicants' amendments and remarks submitted May 15, 2009 have been fully considered, and are found persuasive to overcome the rejections set forth in the prior office action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shengjun Wang/
Primary Examiner, Art Unit 1617

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